UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
08/465,322	06/05/95	SODERLUND	H	A28203-A-FWC

HM31/0603

BRUMBAUGH GRAVES DONOHUE & RAYMOND
30 ROCKEFELLER PLAZA
NEW YORK NY 10112

EXAMINER	
MYERS, C	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 06/03/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant
08/465,322	Soderlund et al
Examiner	**Group Art Unit**
Carla Myers	1634

☒ Responsive to communication(s) filed on *May 14, 1998* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *51-68* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *54-62* is/are allowed.

☒ Claim(s) *51-53 and 63-68* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on May 14, 1998 has been entered.

2. Claim 68 is rejected under 35 U.S.C. 112, second paragraph as indefinite and vague over the recitation of "wherein the oligonucleotide primer is hybridized to the target" because it is not clear as to whether the claimed reagent itself is present in a form in which it is hybridized to the target nucleic acid or if it is only a property of the claimed reagent that it is capable of hybridizing to the target nucleic acid adjacent to the predetermined position.

Applicants state that the claims must be read through the eyes of one of skill in the art and in light of the specification and thereby it is clear what is intended to be meant by the claims. However, there is no limitation in the claims or teachings in the specification which clarify the intended limitation of claim 68. It is maintained that it is not clear as to whether applicants intend to claim a double-stranded hybrid oligonucleotide in which the primer is bound to a target nucleic acid (as is inferred by the recitation that the primer "is" bound to a target nucleic acid) or if applicant intends to claim a

primer that has the property of being capable of binding to a target nucleic acid (as is inferred by the recitation that the claimed reagent is a primer, rather than a product formed by the binding of a primer to a target).

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 51, 53, 64-66 and 68 are rejected under 35 U.S.C. 102(e) as being anticipated by Erlich.

Erlich (see, for example, col. 8) teaches primers useful for the amplification of target nucleic acids containing a variable nucleotide, such as a polymorphism/mutation. Erlich teaches that primers are generated which have the property of hybridizing to the nucleic acid 5' to the nucleotide in the target nucleic acid containing the variable nucleotide, so that extension of the 3' end of the primer results in the addition of a nucleotide complementary to the variable nucleotide. In particular, Erlich teaches primers, for example primer "DB01" (see columns 29 and 30), which hybridize to the target nucleic acid so that the 3' nucleotide of the primer is immediately adjacent to a variable

nucleotide and extension of the primer results in the addition of a nucleotide complementary to a first or second nucleotide residue. It is pointed out that the 3' residue of the DB01 primer flanks the "CTT" codon, which is present as a "GTG" codon in allelic variants and thereby the "C" nucleotide adjacent to the primer is considered to be a variable or mutated nucleotide and the "C" and "G" nucleotides are considered to be a first and a second "nucleic acid residue at a defined site". With respect to claim 53, Erlich teaches that primers may be 15 to 25 nucleotides in length (col. 4) and teaches that the DB01 primer is 21 nucleotides in length (col. 29). With respect to claims 64-66, it is a characteristic of the reagent that it is capable of forming an extension product by incorporation of a labeled deoxribonucleotides or dideoxyribonucleotide.

In the response of Paper NO. 10, Applicants traversed this rejection by stating that Applicants invention does not require the inclusion of a hybridization step to determine if nucleotide variation is present but requires the use of a reagent , i.e. a primer which hybridizes adjacent to the target region. However, the fact that the method of Erlich is different from that of Applicants is not relevant here because the claims are drawn to products and not to methods. A comparison is made only between the product of Erlich and the product of the instant invention. The oligonucleotides of Erlich have the exact same properties as

the reagents of the instant invention. The primer of Erlich, when hybridized to the target nucleic acid, is adjacent to the variable nucleotide, such that extension of the primer at the 3' end results in the incorporation of a variable nucleotide. Applicants attention is drawn to col. 29 and 30 of Erlich wherein the position of the DB01 primer is clearly shown, such that the primer hybridizes 3' to the CTT codon, which consists of a variable nucleotide since this codon may also be present as GTG. Therefore, it is a property of the DB01 primer of Erlich that it hybridizes to a segment of the target adjacent to a variable nucleotide. It is again pointed out that the recitation of the intended use of the primers of the instant invention does not carry weight.

4. Claims 52, 63 and 67 are rejected under 35 U.S.C. § 103 as being unpatentable over Erlich (U.S. Patent No. 5,310,893).

Erlich (see, for example, col. 8) teaches primers useful for the amplification of target nucleic acids containing a variable nucleotide, such as a polymorphism/mutation. Erlich teaches that primers are generated which have the property of hybridizing to the nucleic acid 5' to the nucleotide in the target nucleic acid containing the variable nucleotide, so that extension of the 3' end of the primer results in the addition of a nucleotide complementary to the variable nucleotide. In particular, Erlich teaches primers, for example primer "DB01" (see columns 29 and

30), which hybridize to the target nucleic acid so that the 3' nucleotide of the primer is immediately adjacent to a variable nucleotide and extension of the primer results in the addition of a nucleotide complementary to a first or second nucleotide residue. It is pointed out that the 3' residue of the DB01 primer flanks the "CTT" codon, which is present as a "GTG" codon in allelic variants and thereby the "C" nucleotide adjacent to the primer is considered to be a variable or mutated nucleotide and the "C" and "G" nucleotides are considered to be a first and a second "nucleic acid residue at a defined site". Erlich teaches that primers may be 15 to 25 nucleotides in length (col. 4) and teaches that the DB01 primer is 21 nucleotides in length (col. 29). Erlich does not specifically exemplify a DB01 primer having attached thereto an "attachment moiety" through which the primer can be immobilized or immobilization of the primer and the amplification product onto a solid support. However, Erlich does teach that primers useful for amplifying variable nucleotides can be modified so as to attach labels thereto, including labels which can be used to capture the primer and facilitate immobilization of the primer onto a solid support (see col. 5). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the amplification primer of Erlich so as to have

attached a moiety allowing for the immobilization of the primer in order to have accomplished the expected advantage of generating a primer which could easily immobilized onto a solid support to have allowed for the rapid and efficient separation and isolation of the nucleic acids comprising the amplification primer from other nucleic acids. With respect to claims 64 and 65, it is a characteristic of the reagent that it is capable of forming an extension product by incorporation of a labeled dideoxyribonucleotide.

In the response of Paper No. 10, Applicants traverse this rejection by stating that the Examiner has misunderstood the teachings of Erlich. It is asserted that Erlich doesn't teach a primer for detecting the presence of a specific nucleotide at a predetermined position in a target nucleic acid. Applicants go on to further compare the methodology disclosed in the instant specification with the methodology disclosed by Erlich. However, it is pointed out that the claims are not drawn to methods, but rather are drawn to products. The recitation in the claims of the intended use of the product does not carry weight with respect to the issue of obviousness. The question is only one of whether the instant products are obvious in view of the teachings of Erlich. That is, the comparison is made only between the functional and structural limitations of Applicants product and the product of Erlich. Again, Erlich teaches an oligonucleotide

DB01 primer which hybridizes 3' to the CTT codon, which consists of a variable nucleotide since this codon may also be present as GTG. Therefore, it is a property of the DB01 primer of Erlich that it hybridizes to a segment of the target adjacent to a variable nucleotide. The oligonucleotide of Erlich differs from the claimed oligonucleotide only in that Erlich does not specifically exemplify a DB01 primer having attached thereto an "attachment moiety" through which the primer can be immobilized or immobilization of the primer and the amplification product onto a solid support. However, Erlich does teach that primers useful for amplifying variable nucleotides can be modified so as to attach labels thereto, including labels which can be used to capture the primer and facilitate immobilization of the primer onto a solid support (see col. 5). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the amplification primer of Erlich so as to have attached a moiety allowing for the immobilization of the primer in order to have accomplished the expected advantage of generating a primer which could easily immobilized onto a solid support to have allowed for the rapid and efficient separation and isolation of the nucleic acids comprising the amplification primer from other nucleic acids.

5. Claims 54-62 are allowable over the prior art. While the prior art teaches primers for the amplification of mutations

present in the genes of ApoE, *B*-globin, and ras, the prior art does not lead one to the particularly primers claimed because the prior art does not teach or suggest the generation of primers which are specifically designed so that when the primer is hybridized to the target nucleic acid, the 3' terminal nucleotide of the primer directly flanks the nucleotide at which the mutation is present in the target nucleic acid.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703)-308-1152. The fax number for the Technology Center is (703)-305-3014 or (703)-305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

June 2, 1998

Carla J. Myers
CARLA J. MYERS
PRIMARY EXAMINER